38. (Amended) The composition of claim 36 wherein said vector consists of the nucleic acid sequence of [has] SEQ ID no: 1.

Cancel claims 2 to 5 and 20 to 35.

REMARKS

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of three months of the period for response to the outstanding Office Action on this case. We enclose our cheque in the amount of the prescribed fees.

The courtesy of the Examiner in granting an Interview on this application to the applicant's representative, Mr. Michael Stewart, and to Mr. Reza Yacoob of the Patents Department of the assignee company, is much appreciated. It is considered that the Interview was material in advancing the prosecution of this application. The Interview Summary fairly sets forth the discussion at the Interview. The comments and submissions herein complement and supplement those made to the Examiner at the Interview.

The Examiner indicated that the amendments made to pages 9, 10, 11 and 20 to 26 noted in the Amendment filed April 13, 2000 have not been entered since the text described does not appear on the pages listed. At the Interview, it was ascertained that the page and line number of the Examiner's text differed from that in applicant's file on which the instructions in the Amendment of April 13, 2000 was based. Substitute directions will be given in due course with respect to page and line numbers which, it is believed, correspond to the Examiner's text.

The Examiner indicated that the attempt to incorporate subject matter into this application by reference to U.S. Application No. 08/923,558 is improper on the basis that the method of immunizing the mice is considered essential to practice the invention. In this regard, the Examiner indicated that the relevant information relating to the method of immunizing the control group should be included in the instant specification. It is noted that Application No. 09/923,558 corresponds to the cited Parrington et al reference.

The Examiner noted that the results obtained in Applications Nos. 08/923,558, 08/476,397 and 08/986,500 are not included in the instant specification. Application No. 08/476,397 is now U.S. Patent No. 6,019,980 while Application No. 08/896,500 is now U.S. Patent No. 6,017,897. In any event, the subject matter of

the latter two applications is contained in the cited Li et al reference (WO 96/409450).

All data that is referred to in the specification, particularly Example 3, is contained in documents which are in the public domain. In any event, contrary to the Examiner's suggestion, the immunization protocol from Application No. 08/923,578 is recited therein. As stated, the prime and boost immunizations were effected with 25 μg of RNA injected into each hind leg muscle in 50 μL of P BS. As stated, there was no pretreatment with cardiotoxin. With the exception of the lack of pretreatment with cardiotoxin, this is the same protocol for the same DNA as described in Table I (col. 14) of USP 6,060,308.

Having regard to the above, it is submitted that the specification requires no revision in this respect.

The Examiner noted that the blanks for the U.S. Patent Applications referred to on pages 23 and 24 and the blank for the ATCC designation and date for pMP42 on page 22, should be completed. The directions to amend the specification include completion of this informality.

The Examiner objected to claim 16 for repetition of the term "to". Claim 16 has been amended to remove this informality. The Examiner objected to claim 11 as lacking the term "to" following the term "adjacent" in line 2. This objection is rendered moot by deletion of the claims.

The Examiner rejected claims 1, 2 and 5 to 38 under 35 USC 112, first paragraph, on the basis that, while enabling for immunogenic compositions and a method of provoking an immune response, does not reasonably provide enablement for the vaccine compositions and methods of preventing disease. The Examiner asserted that the specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Claim 1 defines a vector having defined elements while claim 36 defines an immunogenic composition comprising the vector. As discussed at the Interview, it is believed that these claims are enabled, having regard to the Examiner's comments as to subject mater enabled.

While not agreeing with the Examiner's reasoning, claims 20 to 35 have been deleted, such deletion being effected without prejudice to the applicants right to pursue such claims in a continuation application.

Having regard to the above, it is submitted that the claims remaining in the application are fully enabled and hence the rejection of claims 1, 2 and 5 to 38, insofar as they remain in the application and in their amended form, under 35 USC 112, first paragraph, should be withdrawn.

The Examiner rejected claims 1, 2 and 5 to 38 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner raised several specific objections to specific claims:

(a) In claim 1, the Examiner considered the term "a protein or a protein fragment that generates antibodies that specifically react with the paramyoxovirus protein" on the basis that a protein or protein fragment does not generate anything. First of all, the phrase "that generates ..." only governs the term "protein fragment" and is intended to define this fragment in functional terms. To clarify the language the term "encoding" has been inserted prior to "fragment" and the term "generates" has been replaced by the term "induces production of". It is submitted that claim 1 can no longer be considered indefinite in this regard.

(b) Claim 5 has been deleted since the subject matter thereof has been included in claim 1.

(c) The Examiner considered the term "identifying characteristics of plasmid pMP44" is indefinite in claims 18, 21, 33 and 37. Claims 21 and 33 have been deleted and claims 18 and 37 have been amended to refer to the plasmid as being pMP44. It is submitted that claims 18 and 37 can no longer be considered indefinite in this regard.

(d) The Examiner considered the term "adjacent" as used in claim 11 to be indefinite. Claim 11 now has been incorporated into claim 1. While not agreeing with the Examiner's view, the phrase "located

adjacent" has been replaced by "operatively linked" when incorporating the language of claim 11 into claim 1.

(e) The Examiner considered the phrase "to enhance the immunoprotective ability of a paramyoxvirus protein" in claim 11 to be indefinite. Claim 11 has been incorporated into claim 1. The immunoprotective ability of the protein is the ability for a specific dose of the protein to induce a particular immune response. It is submitted that claim 1 is not indefinite in this respect.

(f) The Examiner considered the phrase "when expressed *in vivo* from the vector in a host' as used in claim 11 to be unclear. The subject matter of clam 11 has been incorporated into claim 1. While it is believed the expression to be clear in scope, the language has been amended to specify that the protein is expressed from the vector when this expression occurs *in vivo*. It is submitted that claim 1 can no longer be considered indefinite in this respect.

(g) The Examiner considered the term "substantially" in claim 12 to be indefinite. The phrase has been deleted from claim 12.

(h) The Examiner considered the term "aberrant mRNA splicing, *in vivo*", as used in claim 12 to be indefinite. The misplaced comma appears to be the source of the difficulty and now has been deleted. It is submitted that it is clear that aberrant mRNA splicing does not occur when the vector is used *in vivo*.

(i) The Examiner considered the term "has" in claims 19, 22, 31, 34 and 38 to be indefinite. Claims 22, 31 and 34 have been deleted. Claims 19 and 38 have been amended to refer to the vector consisting of a nucleic acid sequence of SEQ ID No: 1. It is submitted that claims 19 and 38 can no longer be considered indefinite in this regard.

(j) The Examiner raised several objections to claims 20 to 22, 23 to 31, 32, 33, 36, 23 and 21. However, these claims have been deleted, thereby obviating the rejection with respect to such claims.

Having regard to the revisions made to the claims and the above comments, it is submitted that claims 1, 2 and 5 to 38, insofar as they remain in the

application and in their amended form, can no longer be considered indefinite, and hence the rejection thereof under 35 USC 112, second paragraph, should be withdrawn.

The Examiner rejected claims 1, 2, 8, 9, 11 to 13, 18, 20, 21, 32, 33, 35, 36 and 37 under 35 USC 102(e) as being anticipated by Dubensky et al. As noted above, claim 1 has been limited to the subject matter of claim 11 while claims 2, 11, 20 21, 32, 33 and 35 have been deleted.

With respect to the recitation in claim 1 of the third DNA sequence, it is submitted that this feature is not disclosed in Dubensky et al and hence claim 1, as amended, is not anticipated by Dubensky et al. In addition, claim 1 has been limited to the subject matter of claim 5, not the subject of this invention. This amendment renders the rejection moot.

Claim 1 defines a vector which comprises four elements:

- a first DNA sequence which is complementary to at least part of an alphavirus RNA genome replication region that permits *in vivo* replication,
- a second DNA sequence encoding a respiratory syncytial virus (RSV) protein which is selected from a group consisting of the F and G glycoproteins of RSV or encoding an RSV protein fragment that induces production of antibodies that specifically react with the RSV protein, with the second DNA sequence being inserted into a region of the first DNA sequence that is non-essential for replication,
- a third DNA sequence operatively linked to the first DNA sequence and that enhances the immunoprotective ability of the RSV protein or fragment thereof when expression occurs *in vivo*, and a promoter transcriptionally controlling the first, second and third DNA sequences.

In the Office Action, the Examiner comments:

> "The limitation of a third sequence located adjacent to the first sequence and between the first sequence and the promoter (claims 11-13) is equivalent to the DNA sequence adjacent to the alphavirus sequence and the DNA sequence between the alphavirus sequence and the promoter taught by Dubensky et al. Such a sequence comprises a "pair of splice sites" because the sequence can be spliced at any two sites. The phrases "to enhance the immunoprotective ability" and "to prevent aberrant mRNA splicing" are intended uses and do not bear patentable weight when considering art rejections."

As discussed at the Interview, there is no element disclosed in Dubensky et al which is operatively linked to the first DNA sequence and which specifically functions in a manner which enhances the immunoprotective ability of the RSV protein or fragment when experiments of the protein or fragment thereof occurs *in vivo*.

Contrary to the Examiner's suggestion, a functional recitation can define a structural element and serve to distinguish over prior art. In this regard, it is noted that the term "to enhance" in claim 1 (old claim 11) has been replaced by the term "that enhances" and the term "to prevent" in claim 12 has been replaced by "that prevents". It is submitted that such terms are not statements of "intendedness" but rather the specific function of the recited element and should be accorded patentable weight when considering the prior art rejection.

In the event the Examiner maintains the rejection, the Examiner is requested to identify the specific recitation in Dubensky et al of a DNA sequence which corresponds to applicants third DNA sequence.

Having regard to the above and the amendments made to the claims, it is submitted that claims 1, 2, 8, 9, 11 to 13, 18, 20, 21, 32, 33, 35, 36 and 37, insofar as they remain in the application and in their amended form, are not anticipated by the cited prior art and hence the rejection thereof under 35 USC 102(e) as being anticipated by Dubensky et al, should be withdrawn.

The Examiner rejected claims 1, 2, 5 to 16, 18, 20, 21, 23 to 30, 32, 33, 35, 36 and 37 under 35 USC 102(e) as being anticipated by Parrington. As noted above, the subject matter of claims 5 and 11 has been incorporated into claim 1 and claims 2, 5, 11, 20, 21, 23 to 30, 32, 33 and 35 have been deleted.

It is submitted that Parrington does not disclose a vector as claimed in amended claim 1. While Parrington discloses a vector containing the first DNA sequence, the second DNA sequence and the promoter, Parrington does not disclose a vector which contains the third DNA sequence.

In the Office Action, there is stated:

> "The sequence may contain the CMV immediate early promoter and rabbit β-globin intron II (column 4, line 11).

Col. 4, line 11, to which the Examiner refers, is discussing the content of WO 96/40945, i.e., the Li et al reference cited by the Examiner and the vector which is described therein. While the Li et al vector contains the rabbit β-globin intron II sequence, the Li et al reference does not employ a Semliki virus sequence ("first DNA sequence"). There is no disclosure in Parrington of a vector containing the β-globin intron II sequence ("third DNA sequence").

Accordingly, it is submitted that the rejected claims of the application are not anticipated by the cited prior art and hence the rejection of claims 1, 2, 5 to 16, 18, 20, 21, 23 to 30, 32, 33, 35, 36 and 37, insofar as they remain in the application and in their amended form, under 35 USC 102(e) as being anticipated by Parrington, should be withdrawn.

The Examiner rejected claims 1, 2, 5 to 16, 18, 20, 21, 23 to 30, 32, 33, 35, 36 and 37 under 35 USC 103(a) as being unpatentable over Dubensky et al in view of Li et al. The relevance of Dubensky et al with respect to the rejected claims and the manner of distinction thereover have been discussed above in connection with the rejection under 35 USC 102(e).

The Examiner apparently relies on the Li et al reference for the teaching of a vector encoding the RSV F and G proteins under the control of the CMV early promoter and comprising the rabbit globin intron II. The Li et al reference does not contemplate the employment of a Semliki forest virus sequence in any construct and, as noted above, Dubensky et al does not contemplate the rabbit globin intron II or any other equivalent "third DNA sequence" as recited in claim 1.

The Examiner states in the Office Action:

> "Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expression vector encoding RSV proteins taught by Dubensky et al to deliver the F or G protein taught by Li et al. Motivation is provided by Li et al by stating that the F or G proteins may be used to induce an immune response (page 15, line 17)."

While Dubensky et al do not specifically describe any construct which utilizes RSV F and/or G sequence as the heterologous sequence in the eukaryotic layered vector initiator system described therein, it is possible to contemplate such protein as the

antigen of interest. However, until such a structure is assembled, it is not known if the vector will function as intended.

The Examiner goes on to say:

> "It would have been obvious to one of skill in the art at the time of filing to put the rabbit β-globin intron II sequence between the alphavirus sequence and the CMVIE promoter to enhance transcription/translation and increase *in vivo* expression as suggested by Li et al (page 14, line 10)."

It is submitted that there is no motivation provided by Li et al to incorporate the rabbit β-globin intron II into the structure described in Dubensky et al since Dubensky does not contemplate any such sequence in the structure provided. There is no motivation to include such sequence as a "third DNA sequence" at the specific location contemplated by claim 1.

Accordingly, it is submitted that the rejected claims are patentable over the applied prior art and hence the rejection of claims 1, 2, 5 to 16, 18, 20, 21, 23 to 30, 32, 33, 35, 36 and 37, insofar as they remain in the application and in their amended form, under 35 USC 103(a) as being unpatentable over Dubensky et al in view of Li et al, should be withdrawn.

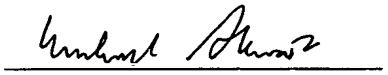
The Examiner rejected claims 1, 2, 5 to 16, 18, 20, 21, 23 to 30, 32, 33 and 35 to 37 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-[unspecified] of U.S. Patent No. 6,060,308.

The relationship of the claims of this application as amended to U.S. Patent No. 6,060,308 has been discussed above with respect to the rejection based upon this reference under 35 USC 102(e). It is submitted, from that discussion, that the claims of this application are patentably distinct from the claims of U.S. Patent 6,060,308.

Accordingly, it is submitted that none of the claims of this application represents an obviousness-type double patenting of any claim of USP 6,060,308, and hence the rejection of claims 1, 2, 5 to 16, 18, 20, 21, 23 to 30, 32, 33 and 35 to 37, insofar as they remain in the application and in their amended form, as being unpatentable over the claims of USP 6,060,308, should be withdrawn.

It is believed that this application now is in condition for allowance and early and favorable consideration and allowance are respectfully submitted.

Respectfully submitted,



Michael I. Stewart
Reg. No. 24,973

Toronto, Ontario, Canada
(416) 595-1155
FAX No. (416) 595-1163